WE CLAIM:

1. A procoagulant-active FVIII protein comprising a human FVIII polypeptide that is modified, wherein the modification comprises a mutation at Phe309.

2. The protein of Claim 1, wherein the mutation is a substitution.

3. The protein of Claim 1, wherein the mutation is a deletion.

4. The protein of Claim 2, wherein the mutation comprises substitution of the Phe with Ser.

5. A nucleic acid molecule comprising a nucleotide sequence that encodes the protein of Claim 1.

6. An expression vector comprising the nucleic acid molecule of Claim 5.

7. A host cell transformed or transfected with the nucleic acid molecule of Claim 5.

8. A pharmaceutical composition comprising an effective amount of the protein of Claim 1 in admixture with a parenterally acceptable vehicle or excipient.

9. A method for the production of a procoagulant-active protein comprising the steps of:

a) growing, in culture, a host cell transformed or transfected with the nucleic acid molecule of Claim 5; and

b) isolating from said host cell and culture, the polypeptide product of the expression of the nucleic acid molecule.

10. A procoagulant-active FVIII protein comprising a human FVIII polypeptide that is modified, wherein the modification comprises a substitution of the Arg residue at position 336 with Ile and a substitution of the Arg residue at position 562 with Lys.

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11. The protein of Claim 10, wherein the modification further comprises a mutation at Phe309.

12. A nucleic acid molecule comprising a nucleotide sequence that encodes the protein of Claim 10.

13. A pharmaceutical composition comprising an effective amount of the protein of Claim 10 in admixture with a parenterally acceptable vehicle or excipient.

14. An expression vector comprising the nucleic acid molecule of Claim 12.

15. A host cell transformed or transfected with the nucleic acid molecule of Claim 12.

16. A method for the production of a procoagulant-active protein comprising the steps of:

a) growing, in culture, a host cell transformed or transfected with the nucleic acid molecule of Claim 12; and

b) isolating from the host cell and culture, the polypeptide product of the expression of the nucleic acid molecule.

17. A procoagulant-active FVIII protein comprising a human FVIII polypeptide that is modified, wherein the modification comprises a deletion of the B domain, a deletion of the von Willebrand factor binding site, a mutation at Arg740 and an addition of an amino acid sequence spacer between the A2- and A3-domains.

18. The protein of Claim 17, wherein the modification further comprises a substitution of the Arg residue at position 336 with Ile and a substitution of the Arg residue at position 562 with Lys.

19. The protein of Claim 17, wherein the modification further comprises a mutation at Phe309.

20. The protein of Claim 17, wherein the mutation comprises a substitution of Arg at position 740 with Ala.

21. The protein of Claim 17, wherein the amino acid sequence spacer is 54 residues in length.

22. The protein of Claim 21, wherein the amino acid sequence spacer comprises residues 741 to 794 of wild-type FVIII, wherein the residue at position 794 is selected from the group consisting of threonine and leucine.

23. The protein of Claim 22, wherein the residue at position 794 is threonine.

24. A nucleic acid molecule comprising a nucleotide sequence that encodes the protein of Claim 17.

25. An expression vector comprising the nucleic acid molecule of Claim 24.

26. A host cell transformed or transfected with the nucleic acid molecule of Claim 24.

27. A pharmaceutical composition comprising an effective amount of the protein of Claim 17 in admixture with a parenterally acceptable vehicle or excipient.

28. A method for the production of a procoagulant-active protein comprising the steps of:

a) growing, in culture, a host cell transformed or transfected with the nucleic acid molecule of Claim 24; and

b) isolating from the host cell and culture, the polypeptide product of the expression of the nucleic acid molecule.

FORTHCOMING

29. A method of increasing binding of the protein of Claim 17 to von Willebrand factor in plasma comprising the step of introducing in plasma containing the protein and von Willebrand factor, an antibody or cross-linking agent which increases the protein's binding affinity to von Willebrand factor.

30. The method of Claim 29, wherein the antibody recognizes an epitope at amino acids 2248 to 2285 of the protein.

31. The method of Claim 30, wherein the antibody is ESH8.

32. A procoagulant-active FVIII protein comprising the A1-, A2-, A3-, C1- and C2- domains of human Factor VIII, characterized in that upon thrombin activation, the protein becomes a heterodimer comprising an A1- domain fragment and an A2-A3-C1-C2 chain.

33. A nucleic acid molecule comprising a nucleotide sequence that encodes the protein of Claim 32.

34. An expression vector comprising the nucleic acid molecule of Claim 33.

35. A host cell transformed or transfected with the nucleic acid molecule of Claim 33.

36. A pharmaceutical composition comprising an effective amount of the protein of Claim 32 in admixture with a parenterally acceptable vehicle or excipient.

37. A method for the production of a procoagulant-active protein comprising the steps of:

a) growing, in culture, a host cell transformed or transfected with the nucleic acid molecule of Claim 33; and

b) isolating from the host cell and culture, the polypeptide product of the expression of the nucleic acid molecule.

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38. A method of increasing binding of the protein of Claim 32 to von Willebrand factor in plasma comprising the step of introducing in plasma containing the protein and von Willebrand factor, an antibody or cross-linking agent which increases the proteins binding affinity to von Willebrand factor.

39. The method of Claim 38, wherein the antibody recognizes an epitope at amino acids 2248 to 2285 of the protein.

40. The method of Claim 39, wherein the antibody is ESH8.